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May 8, 1970

W. E. HILTON
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TOXICOLOGICAL INFORMATION ON $C_8$ APFC

I'm sorry for the delay in replying to your recent request for an evaluation of employee hazard from $C_8$APFC in your polymerization operations. I hope this letter will sufficiently amplify my telephone comments of April 16.

As I understand it, you currently are using $C_9$APFC, but are phasing it out and will be using $C_8$APFC for ca. 80 per cent of the Teflon® polymerizing and chlorendic acid for the other 20 per cent. AHT is not used.

I have summarized the available toxicity information on $C_8$APFC and chlorendic acid in the attached table. We have even less information on $C_9$APFC and some of it is internally conflicting. The information is inadequate for a complete evaluation of the toxicity of these materials. Your principal exposure is by skin absorption. We have no skin absorption toxicity information on any of the three. $C_8$APFC and $C_9$APFC cause liver enlargement, but we don't know what is the lowest repeated oral dosage that will cause it. We have no repeated oral dosage study to indicate if $C_8$APFC or $C_9$APFC accumulates in the body to toxic levels. We do not know the eye or skin irritation potential for $C_8$APFC or $C_9$APFC and we do not know whether the liver enlargement effect occurs only in rats or in other species as well. Except for the knowledge that chlorendic acid does not cause liver enlargement, our data for this material are similarly sketchy. We have no information on the toxicity of disuccinic acid peroxide.

To answer the initial toxicity questions on $C_8$APFC, I suggest the following tests:

I. Determination of lethal concentration by single oral doses and determination of lowest oral dosage causing liver enlargement in rats (histopathology of liver only). $600

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| II. | Accumulation in the rat to cause liver enlargement (two-week subacute, oral dosing). | $ 750 |
| III. | Accumulation in the rat to lethal levels (with histopathologic examination of tissues, oral dosing). | $1400 |
| IV. | Recovery study for regression of liver enlargement in the rat after oral dosing. | $1000 |
| V. | Single administration skin absorption toxicity (this is done in the rabbit and can be done with enough rabbits to measure liver enlargement). | $ 800 |
| VI. | Repeated application skin absorption study without histopathology but with examination of livers. | $1500 |
| VII. | Primary skin irritation and sensitization (this is done in the guinea pig and can be done with enough guinea pigs to determine if there is significant liver enlargement). | $1200 |
| VIII. | Eye irritation. | 300 |
| IX. | Repeated (two-week) inhalation administration with histopathology. | $2000 |
| X. | Coordination of the above program, interim reports and final evaluation. | +15% |

The liver enlargement evaluation in the above studies has not added materially to the cost. In addition, we recommend a 90-day feeding study in rats and dogs including a one-generation reproduction-teratogen study in rats. This would cost ca. $30,000. This study is recommended because we have no chronic studies on any of these surfactants and no adequate studies in non-rodent species. Depending on the results of this 90-day study, a protracted study in dogs or dogs and rats, might be indicated.

None of the above studies would allow us to set an atmospheric level of CRAPFC that would be hygienically acceptable on a chronic basis. This would require a chronic inhalation study. The exact cost would depend on final test design, but it would be in excess of $100,000.

May 8, 1970

If you can eliminate continuous exposure to $C_8APFC$ by inhalation, none of the repeated inhalation studies would be necessary. Similarly, elimination of repeated exposure by skin absorption would eliminate the need for a repeated skin absorption toxicity study. I suggest a visit by our industrial hygienist, Mr. Morgan, as the most beneficial next step to determine the extent of the toxicity testing program. This would also give us better insight into developing the necessary toxicity testing program for chlorendic acid.

RSW

RICHARD S. WARITZ
RESEARCH MANAGER, BIO-SCIENCES GROUP

RSW:ljm
Attachment

## SUMMARY OF TOXICITY DATA[δ] ON $C_8$APFC AND CHLORENDIC ACID

| Test | $C_8$APFC | Chlorendic* Acid | Chlorendic* Anhydride |
|---|---|---|---|
| Oral Approximate Lethal Dose | 670 mg/kg | 5000 mg/kg** | 1000 mg/kg not lethal |
| Oral liver enlargement | 60-90 mg/kg | No | No |
| Oral Subacute | ND | 8 x 1000 mg/kg caused seven deaths (10 rats used) | 8 x 1000 mg/kg caused six deaths (10 rats used). |
| Approximate Lethal Dose | 0.8 mg/L (caused liver enlargement) | ND | ND (Respiratory irritant in rats). |

ND - Not determined
* - Data from Hooker Chemical
** - Haskell Laboratory found 2250 mg/kg
δ - On rats only

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